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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,237	01/25/2002	Richard Wisniewski	2035749	8952

7590 06/02/2004

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EXAMINER	
FORD, JOHN K	

ART UNIT	PAPER NUMBER
3753	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/056,237	WISNIEWSKI ET AL.	
	Examiner	Art Unit	
	John K. Ford	3753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 7/14/03 & 3/5/04

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) 1-42 is/are pending in the application.

4a) Of the above claim(s) 9-26 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) 1-8 and 27-42 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' responses of July 14, 2003 and March 5, 2004 have been studied carefully. The First and Second declarations by Mr. Wisniewski are now properly of record. As indicated however the text of at least one of these documents refers to office actions in other applications rather than the current one. To the extent that those remarks are still germane to the rejections set forth here they are treated here. Declarations by Burman, Lawlis, Jr. and Vetterlein are not yet of record here, but are treated nonetheless, given that they have been made of record in other closely related applications.

It is noted for the record, as recently as the year 2000, Mr. Wu and Mr. Wisniewski co-authored a publication entitled: "Scale-Down approach to Large Volume Cryopreservation of Biopharmaceuticals using the CryoCassette and CryoWedge."

It is noted for the record as a fact that in this prosecution, progressively, more and more information about the Genentech device has been provided by Mr. Wisniewski as he has been repeatedly asked questions about it. Problematic of this creeping disclosure, it is noted that the 1992 Wisniewski and Wu article was not originally provided to the Examiner by Applicants. Instead, a far less detailed description of the Genentech device was provided in the 1996 article by Wisniewski and Wu entitled "Large-Scale Freezing and Thawing of Biopharmaceutical Products". It was only after the Examiner required, on his own, a copy of a reference identified on page 59 of the aforementioned article that a copy of it was finally produced.

As time has gone on, continued questioning by the Examiner has led to Mr. Wisniewski revealing many more details about the Genentech device through

declarations and statements in the record. In the face of all of this additional evidence produced by the Examiner's questions, counsel now asserts, in at least one other closely related application, with no logic or reasoning, that applicants (Mr. Wisniewski and Mr. Leonard, who has not gone on record in any declaration) have fully complied with Rule 56, and that Examiner, in pursuing what has thus far been arduous but critically fruitful questioning, is outside his authority.

Applicants have refused to provide the Examiner with any sketch of the prior art discussed on page 2 of the specification. References to two U.S. patents (USP 2,441,376 and 2,129,572) which have nothing to do with freezing biopharmaceuticals and that applicants were unaware of at the time that the specification was written does not satisfy the requirement.

The Examiner needs to have full disclosure of the Genentech device to properly consider the patentability of the current claims. But for Mr. Wisniewski's close connection to Genentech, and the 1992 article, the Examiner has no other reasonable source of information. Rule 56 and Rule 105, (MPEP 704.10) in particular, empower the Examiner to make inquiries and unfortunately Applicants have provided the information about the Genentech device in dribs and drabs over the course of years, leading to protracted questioning which is no more pleasant for the Examiner than for applicants. It is unfortunate that applicants have chosen this route but the questioning would have long ago ceased if the relevant information was provided completely at the beginning of the prosecution.

Extremely relevant prior art is discussed in the specification under the heading "2. Description of the Prior Art" (specification, paragraphs 0003-0005). Unfortunately the description is somewhat ambiguous. Carefully drawn sketches of this prior art (if no publication exists) have been required for years (in the parent application and other applications being prosecuted in parallel with this one) showing this prior art with enough details so as to permit meaningful comparison to what is claimed here.

Interpretation of claim language

Applicants have argued that the term "biopharmaceutical product" is definite (Paper No. 5 pages 4-8). The Examiner disagrees and further explanation is given below. Counsel calls the Examiner's attention to declarations not of record in this application. If counsel wishes to make them of record here the Examiner will consider them formally. The Examiner has given counsel ample opportunity to make these materials of record and, in not doing so, will have to live with the consequences. It is noted for the record that the definition advanced by those declarants does not supercede what the specification discloses. Counsel criticizes the Examiner's statement, based on reasonable scientific reasoning, suggesting the freezing characteristics of large molecule/cellular solutions of blood and orange juice are more akin to one another than the freezing of ionic buffer solutions (e.g. salts etc.) as "unsupported." Then, counsel says nothing to contradict the Examiner's understanding. This is argument for argument's sake. It does nothing to advance prosecution. Counsel

makes a series of allegations, completely unsupported by facts, suggesting that there are no concerns similar to those disclosed in specification in the freezing of other substances such as milk orange juice etc. This contradicts the discussions found in the prior art references relied upon by the Examiner and is therefore unpersuasive. Moreover in the paragraph spanning pages 6 and 7 counsel alleges that in the "biopharma vocabulary" a "buffer solution" means something other than what it means in a chemistry lab. This sounds like a completely self-serving statement. If it was true why didn't declarants mention it in their declarations?

It is noted that claims 1-8 and 27-34 only claim "actively cooling" the wall and heat exchange structure within the vessel. Claims 35-42, by contrast, claim "actively cooling" the wall and the heat exchange structure and freezing the medium.

Applicant's first and second declarations have been received (on March 5, 2003 and June 14, 2003, respectively). In addition, applicant and counsel have stated for the record (in at least SN 10/057,610) that they will not contact Genentech (Mr. Wisniewski's former employer) to obtain additional information about the prior art 1992 biopharmaceutical freezer that Mr. Wisniewski (and, apparently, Mr. Wu) developed during his employment at Genentech. In refusing the Examiner's request to obtain the relevant dimensions of this prior art device, counsel has stated that it is "unnecessary and goes beyond the duty owed to the Patent Office by an inventor or their representatives." The Examiner will not make any further inquiry in light of this refusal,

as apparently it would be fruitless. The tiresome inquiry has thus far yielded a few additional details from Mr. Wisniewski (e.g. the 1992 article and the 1996 Advanstar Reprint which were not originally submitted to the PTO, only the 1996 DMT article was, and the second declaration paragraph 8 admission that "I know that this distance was greater than 4 inches"), but has largely exceeded in wasted examination time what was extracted in terms of additional details about the prior art, with the exception of the 1992 article and the 1996 Advanstar equivalent.

Mr. Wisniewski's first declaration: Alleged proof of difference between Genentech device and current claimed device

Applicant has stated that no thermal transfer bridge will form in a device with too large a gap (presumably referring to the 1992 Genentech prior art from Basel, Switzerland) between the wall and the tip of the fin connected to the centrally mounted heat exchange structure. The "proof" of this alleged fact is offered in the form of a declaration by one of the inventors (Mr. Wisniewski). With regard to Exhibits B, C and D he states that the temperature distributions shown there "reasonably resemble" the actual temperature profile, "to the best of his knowledge".

There is no evidence that these are actual measured results (the best form of proof in this particular case) or are even computer-generated results. No disclosure is given for the materials and sizes of the components depicted. No disclosure of the gap

size is given in Mr. Wisniewski's analysis. No disclosure is given for how Mr. Wisniewski determined these curves. No calculations are shown. No factual supporting materials are given to support that Mr. Wisniewski's estimates or guesses at the temperature profiles are in fact reflective of reality. The proof as it stands is not convincing as will be elaborated upon below.

Particularly unconvincing in the Examiner's mind is Exhibit D, where ice has clearly bridged the distal end of the heat transfer fin and the inner side of the annular cooled wall.

At that point, Fourier's law of heat conduction essentially begins to take over, and the temperature profile as time goes on will begin to have linearly downward slope determined by the difference in temperature between the distal end of the fin and the inner side of the annular wall.

It is noted, for the record, that Figure 3b of the drawings depicts the temperature profile at some undisclosed time after immediately after cooling has been initiated. It is submitted that immediately after cooling is initiated, for the geometry shown in Figure 3b of the specification, the characteristic "peak-shaped" temperature profile depicted in Exhibits B and C will apply to Applicant's device, because of self-evident principles of heat transfer.

As has been stated by the Examiner, there is really no difference in the fundamental heat transfer physics which occurs in applicant's device of Figure 3B and that depicted in the 1992 publication.

The bridging will admittedly occur more quickly in a small gap than in a large gap, but the temperature profile once enough material is frozen in and around the gap will have a linear profile whose slope is entirely determined by the relative temperatures at the end of the fin and the inside of the wall.

Moreover this Examiner who holds a masters degrees in Engineering from Princeton University, does not believe that there is anyone who can model or calculate these temperature profiles without the aid of sophisticated computers and/or experimental work. On this point see Kalhori & Ramadhyani "Studies on Heat Transfer From A Vertical Cylinder, With or Without Fins, Embedded in a Solid Phase Change Medium", page 44, second and third paragraphs. The processes of modeling natural convection and moving-front phase change occurring together with sub-cooling is, to the Examiner's knowledge, is state of the art or beyond the state of the art in numerical solutions on computers. If applicants know otherwise please submit appropriate proof.

Paragraphs 1 – 4, no dispute.

Paragraph 5, the 1992 and its equivalent 1996 Advanstar publications were not disclosed to the PTO originally. Only a 1996 DMT article was disclosed which contains very few details of the prior art Genentech device. Only through the Examiner's inquiring was the 1992 article and its 1996 Advanstar equivalent made of record.

Paragraph 6, Mr. Wisniewski admits that he designed the internal heat transfer coil with fins for the Genentech device, the details of which he does not, now, recall. While the 1992 article does not explicitly discuss a "thermal bridge" there is nothing, which suggests one did not form. The absence of any specific discussion is not necessarily evidence that the phenomena did not take place. It is respectfully submitted that a thermal bridge would inherently form in the 1992 Genentech device because the vessel wall during the chilling process will always be at a lower temperature that the central structure because the coldest coolant is directed to the jacket first and then the (now slightly warmed coolant) is directed to the central structure by virtue of the piping system clearly disclosed in the 1992 article.

Paragraph 7. Mr. Wisniewski's projections are no more than guesses of what the temperature distribution would be. It is respectfully submitted that these freezing phenomena are so complex that no human being including one with nearly 30 years of experience can accurately predict such results. Purporting to have such ability only diminishes ones credibility. One need not look far to see that the Examiner is correct.

The Kalhori and Ramadhyani (K & R) article, which involves solid phase change around a structure somewhat simpler than the 1992 Genentech device states:

"As will shortly become evident, the problem of phase change around an embedded vertical cylinder is a moving boundary problem in a complex geometry. An analysis of the problem would involve the solution of the energy equation coupled with hydrodynamic equations in the liquid phase. This is a challenging task that is amenable ***only*** to a numerical solution. Consequently, in addition to providing information of utility in the design of thermal storage units, data from the present study could be useful in validating a numerical solution of the problem." (emphasis supplied).

Thus, researchers, other than Mr. Wisniewski, state that accurate modeling of phase change heat transfer in tanks with finned element such as shown in Figure 3 of the K & R article can only be done by computers or by direct empirical measurement.

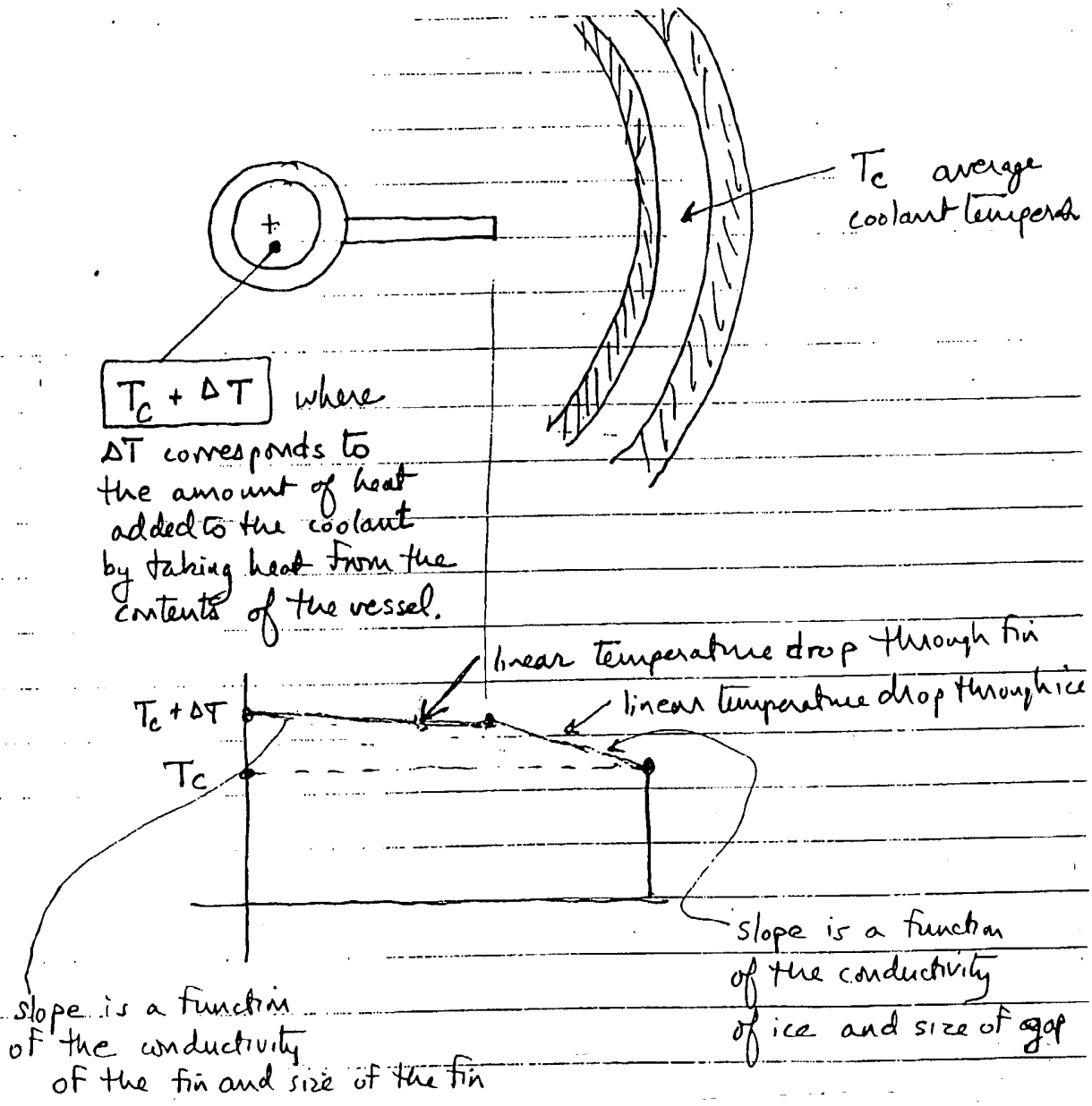
For this reason the Examiner does not find Mr. Wisniewski's thought experiments as credible evidence of what the actual temperatures are in the 1992 Genentech device. The Examiner has repeatedly asked Mr. Wisniewski to test this prior art, or a reasonable facsimile of it, using temperature transducers and Mr. Wisniewski has refused thus far.

Moreover, Exhibit B incorrectly assumes the temperature in the pipe is the same as the temperature in the jacket. This is an incorrect assumption and will necessarily lead to inaccurate conclusions. The temperature in the pipe is a complex function of the initial temperature of the coolant before it passes through the jacket, the temperature of the liquid in the container and the flow rate of the coolant among other variables. As explained above, and as shown in Figure 1 (page 134) of the 1992 article, the coolant goes from the refrigeration system to the jacket and only after exchanging heat with the contents of the vessel (and thereby acquiring some higher temperature) does it pass into the central structure where it necessarily must have a higher temperature than the coolant in the jacket. Thus, Mr. Wisniewski's thought experiments are flawed because they are based on incorrect boundary conditions.

Paragraph 8, Exhibit C, like Exhibit B is simply a guess at what the temperature distribution actually is. As stated with respect to Exhibit B, the temperature distribution must either be measured or generated by very sophisticated computer programs, which have had their validity checked against measured data. Mr. Wisniewski has not done this. The results are not credible, for this reason.

Paragraph 9, Exhibit D is clearly erroneous, beyond the reasons stated above. Once the ice bridges the entire gap to a significant extent, the temperature distribution through a solid ice (non-moving interface) is relatively easy to predict analytically and

Mr. Wisniewski's analysis can be shown to be incorrect. The correct analysis to a first approximation, which can be done by anyone of ordinary skill in the art, is given below:



Paragraph 10, these allegations are not supported by valid factual materials. Mr. Wisniewski's guesswork even in declarative form is simply no substitute for real

evidence. Neither he nor any other person on the planet is in a position to properly guess at the actual temperature distribution. The analysis in paragraph 10 is true no matter how large the gap is. Initially heat will be transferred from the fluid in the gap to both the fin and the wall, regardless of gap size. This process will persist longer in a large gap than a small gap but the physics of the problem is the same regardless of gap size. Applicant is free to rebut this analysis with real evidence (i.e. test results) not idle speculation.

Mr. Wisniewski's Second Declaration

Paragraphs 1 – 4, no dispute.

Paragraph 5, Mr. Wisniewski did not disclose the 1992 article or its 1996 equivalent until the Examiner required its disclosure. Moreover Mr. Wisniewski continues to co-write articles with Mr. Wu including an article written in 2000 entitled "Scale – Down Approach to Large Volume Cryopreservation of Biopharmaceuticals Using the CryoCassette and CryoWedge" (available at Integrated Biosystems website). Mr. Wisniewski has not contacted Mr. Wu to see what he remembers about the Genentech device in spite of repeated requests by the Examiner for additional information.

Paragraph 6, appears to refer to an office action in another application. It is on this basis disregarded.

Paragraphs 7 and 8, for the reasons stated previously, it defies imagination that Mr. Wisniewski could remember the tip to wall distance as greater than 4 inches yet recollect nothing else about the prior art including the approximate size of the vessel (i.e. whether or not he could get his arms around it or pick it up etc.). It is also not understood why he doesn't contact Mr. Wu with whom he co-wrote an article as recently as the year 2000 to see what he remembers of the Genentech device, nor is understood why Genentech would not cooperate given that Genentech is a customer of Integrated Biosystems according to John H. Brown the president and CEO of Integrated Bio Systems (in an article from the wall Street journal available at Integrated Biosystems website). Counsel has gone on the record (Paper No. 8, page 2 in SN 10/057,610) stating that Genentech is a competitor of Integrated Bio system, an allegation, offered as fact that does not appear to comport with reality. The remainder of the factual allegations in paragraph 8, which reiterate those made in the first declaration, are not credible for the reasons enumerated in the Examiner's critique of the first declaration.

Finally, as demonstrated by the article in BioPharm, Vol. 15, No. 5, May 2002 (available at Integrated Biosystems website), Mr. Wisniewski and his assignee have very sophisticated software and hardware at their disposal to perform the testing that the Examiner believes is required to establish the truth of the matter asserted. On page

4 of that article a CryoWedge 20 is disclosed which appears to be used to do the sophisticated type of testing that has been studiously avoided in these applications. If Mr. Wisniewski's hand drawn sketches were accurate it is submitted that Integrated Biosystems would have no need for the Cryowedge 20 or any of the other sophisticated models and programs discussed in that article. It is also noted that Genentech is disclosed to be a customer of Integrated Biosystems not a competitor as alleged by counsel in his latest remarks (Paper No. 8, page 2, paragraph 2, line 6 of SN 10/057,610) calling the Genentech prior art "a competitive system." Note John Brown, in the Wall Street Journal interview, called Genentech a customer of Integrated Biosystems. Each of these units according to Mr. Brown can cost upwards of $ 40,000 - $100,000. With those kinds of numbers and the sophisticated modeling and equipment to perform experiments that exist at Integrated Biosystems the Examiner is completely perplexed with Mr. Wisniewski's and counsel's representations that the PTO has to accept Mr. Wisniewski's hand drawn sketches based on speculative guesswork involving dubious assumptions as the best evidence applicants' possess. Clearly applicants are in a position to present much more legitimate evidence of actual temperature profiles in both their own device and in the prior art than what they have disclosed here.

Given all of the other information that has been given which is incorrect the Examiner does not see how it is possible for Mr. Wisniewski to remember that the fin tip to wall distance was greater than 4 inches yet fail to recall any other relevant dimension

of the prior art (with the same degree of imprecision) including the overall size of the tank. It does not seem plausible to the Examiner. Paragraph 8 is contradicted by the 1992 article where it is explicitly states that the fins were there to form compartments. Mr. Wisniewski's statements that they were only there to increase heat transfer contradict the 1992 article and are not credible. The conclusion, unsupported by any facts, that no thermal bridge was formed in the 1992 Genentech device is similarly not credible.

In paragraph 9, Mr. Wisniewski has simply refused to provide a sketch of the admitted prior art in the parent applications as required numerous times throughout the prosecution. Instead USP 2,441,376 and USP 2,129,572 (references that Mr. Wisniewski was not even aware of at the time that the parent applications were written) are offered instead. Please comply with the sketch requirement. These two references do not correspond to what is disclosed to be the prior art in col. 1, line 33 – 47 of USP 6,196,296, counsel's and applicant's statements to the contrary notwithstanding. The Examiner did not ask about the prior art where the fin was attached to both walls. The Examiner asked for a specific sketch and it has not been produced.

Finally, in paragraph 10, Mr. Wisniewski simply states a conclusion without any legitimate testing to support it. Once the medium is frozen in the gap, the Genentech device will have a "thermal bridge" formed given how that term is defined in the current specification and that of the parent applications.

Definition of biopharmaceutical

The definition of "biopharmaceutical product" offered by Burman, Lawlis, Jr. and Vetterlein is fine as far as it goes but it appears to conflict with the one offered in the specification because some of the examples given in the specification, most notably "buffer solutions" do not fit the definition offered up by Burnam, Lawlis, Jr. and Vetterlein. On this last point, applicant argues that "blood or other body fluids" are buffer solutions and "are indeed biopharmaceutical products due to mixtures of weak acids and base present in them" (remarks, sentence bridging pages 11 and 12). The argument is unconvincing. The Examiner has never heard of "blood" being a known as a buffer solution. Buffer solutions, it is respectfully submitted, are known in the art to be weak acids or bases of known pH used in chemical laboratories. If blood was a known "buffer" why is it (along with "plasma") given as a separate example of a "biopharmaceutical product" in the list found on page 7, lines 4-9?

In response to this action please submit factual materials to support the assertion that "blood" is known to those of ordinary skill to be an example of a "buffer solution".

In paragraphs 0003-0005 of the specification under a section entitled "Description of the Prior Art" applicants appear to disclose that liquids, possibly biopharmaceuticals, have been heated and cooled in containers, which have structures

comprising "extensions of the container or any structures in the container". Fins are mentioned specification under a section entitled "Description of the Prior Art" applicants appear to disclose that liquids, possibly biopharmaceuticals, have been heated and cooled in containers which have structures comprising "extensions of the container or any structures in the container". Fins are mentioned specifically but are "typically attached to the container or an internal structure at only one point".

Full disclosure of this prior art is needed. If applicant does not have a publication, a carefully drawn sketch with meaningful legends and explanations is required. Disclosure of what processes (e.g. heating, cooling, freezing etc.) have been performed in this acknowledged prior art described on pages 2 and 3 of the specification is required as well as what fluids (e.g. biopharmaceuticals etc.) have been processed in the acknowledged prior art container.

Moreover the 1992 disclosure of Wisniewski and Wu does not disclose how close to the wall of the container the heat transfer fins extended, the dimensions of those fins (length, width, height and thickness), the diameter of the container and the volume of the container. Because applicants are in possession of this information and the examiner has no other reasonable way to obtain it, a requirement under Rule 1.56 and Rule 1.105 is set forth here. Timely submission of this information will permit an orderly examination and will avoid the Board having to require such information under Rule

1.196(d) should an appeal be forthcoming. Applicant must know this information because he apparently used it to generate Exhibits B, C and D.

The term "biopharmaceutical product" as it is used in this application is ambiguous and hence its use in the claims is also the source of ambiguity. In contrast with what may be accepted "biopharmaceutical products" such as a product derived from biological sources that has an intended therapeutic application and whose manufacturing is or will be regulated by pharmaceutical or veterinary regulator agencies (in '132 declarations not of record here), in the specification applicants state that the present invention can be used to "freeze and preserve a variety of biopharmaceutical products, including but not limited to proteins, cells, antibodies, medicines, plasma, blood, buffer solutions, viruses, serum, cell fragments, cellular components, and any other biopharmaceutical product".

Many of the purported biopharmaceuticals on applicants' list in the specification are not normally considered biopharmaceuticals on applicants' definition (offered up in the '132 declarations not of record here) above. For example, buffer solutions are acids or bases-dissolved in water not derived from biological sources nor regulated by FDA to the Examiner's knowledge. Blood, per se, such as is drawn from the general population by the Red Cross would not appear to be a biopharmaceutical by affiant' definition yet it appear on applicants' list. On page 133, col. 1, fourth full paragraph, of the 1992 Wisniewski and Wu prior art, it states that "buffer salts" can be components of a

biopharmaceutical product but it appears the "buffer salts" are not themselves a biopharmaceutical product. "Medicines" are simply understood to be drugs or other agents used to treat disease or injury. They need not be derived from biological sources. What is vital to this examination is to know with reasonable particularity what chemicals when placed in applicants' tank would infringe the claims. Under applicants' expansive definition of biopharmaceuticals into the specification it would appear that many conventional organic and inorganic solutions (e.g. buffer solutions) would be included-against what affiant Arathoon, Burman, Lawlis and Vetterlein would consider to be the reasonable limits of the word. On the other hand, orange juice recently shown to have measurable effects against certain forms of cancer, was suggested by counsel to not seriously be considered a biopharmaceutical. The Examiner disagrees. If buffer solutions are considered to be biopharmaceuticals and blood, per se, drawn from the general population a biopharmaceutical, it doesn't seem reasonable to exclude orange juice. The chances of the FDA regulating "buffer solutions" as pharmaceutical in the future would be about on par with the chances of the FDA regulating orange juice as a biopharmaceutical in the Examiner's opinion. If the definition now includes orange juice based on new research showings its anticancer properties and possible future regulation by the FDA, then applicants' use of the word biopharmaceutical seems to include an ever growing and somewhat amorphous list of chemicals what would be perpetually changing as new research was done to show therapeutic properties to products produced by biological processes such as photosynthesis, fermentation and biological agents such as herbs, roots and compound which are essentially the products

of nature. It is impossible to know which of these will be regulated by the FDA in the future given the vicissitudes of government regulation. The term as it is used in the application is deemed by the Examiner to be one that violates the tenets of 35 USC 112, second paragraph, in that the metes and bounds of the claims cannot be established with the requisite clarity required by the statute and are subject to change based on future FDA actions. The would-be infringer would have no clear way to determine infringing behavior, to put it another way. Infringement would be constantly changing depending on what the FDA decided to regulate as a biopharmaceutical. It is noted that the FDA regulates the handling and composition many food items, but that doesn't transform them into biopharmaceuticals even if those food items have some therapeutic benefit. The definition offered by the declarants appears to be unworkable in the Examiner's opinion and that offered in the specification ambiguous.

The declarations under Rule '132 by Arathoon, Burman, Lawlis and Vetterlein (not of record here) all appear to define"biopharmaceutical products" much more narrowly than the expansive definition given in the specification. For example, the Examiner knows of no biologically sourced "buffer solution" which in and of itself is regulated by the FDA. Moreover, it there were such a solution, why would it freeze any differently than a buffer solution not regulated by the FDA nor biologically sourced? It is noted that there is a tremendous variety of "biopharmaceutical products" in applicant's list some of which are very large: cells (e.g. blood etc.) whereas others are millions if not billions of times smaller (e.g. viruses or salt ions in a buffer solution). It is submitted that

the freezing characteristics of solutions at these two extremes would be extremely different. Blood would probably freeze more in the manner of orange juice or milk given its nearly macroscopic cellular nature whereas virus in a suitable butter solution or water would freeze in the manner of pure or salty water. Affiant Arathoon, Burman, Lawlis and Vetterlein all state in their conclusions that Cothern, Nakamura and Morrison (disclosing orange juice, solid particles in a liquid carrier and milk, respectively) do not suggest or teach devices or methods useful in processing biopharmaceutical products. Lacking in any of the declarations is any supporting reasons or analysis to show why declarant Arathoon, Burman, Lawlis and Vetterlein hold this opinion common to all of them. None of the affiant have provided any facts to support such a sweeping conclusion. Moreover Applicants' response as well as the declarations under Rule'132 have failed to reconcile the definition of "biopharmaceutical products" stated in the declarations with the disclosure of the chemicals and blood products, medicines, buffers etc. offered up as examples of biopharmaceutical products clearly encompasses more chemicals than Affiant' declarations under Rule '132. To the extent that the Rule '132 declarations define the term 'biopharmaceutical product" more narrowly than what is disclosed in the specification, the declarations serve to heighten the ambiguity of the disclosed and claimed "biopharmaceutical products" and what the limits (metes and bounds) of that terminology is to have as claim limitation. Moreover, in regard to the cited prior art, nothing in the declarations has addressed why one designing freezing equipment of the chemicals disclosed in the specification would not look to the art of freezing water, orange juice or solids suspended in liquids.

Applicant's traverse of the 35 USC 103 rejections of claims 1-8 and 27-42 based on the prior art.

Counsel admits that none of the claims call for forming a "thermal transfer bridge" on page 9, lines 2 – 11 of the remarks section of the July 14, 2003 response and therefore none of the prior art needs to teach this. Instead he argues that the "dual flow conduit" permits the solution to freeze from the bottom up. Like the thermal bridge that is not claimed, none of the claims require the solution in the tank to be frozen from the bottom up therefore this line of argument is simply incommensurate with the scope of the claims. Moreover this bottom up freezing is explicitly discussed in the text of the 1992 Wisniewski and Wu article and has nothing to do with the dual flow conduit, because the 1992 Wisniewski and Wu article doesn't disclose one. The Examiner is not suggesting that the center mounted heat exchange structure is not a factor in producing the bottom-up freezing, but rather than a host of other (unclaimed) factors such as the freeze jacket extending across the bottom of the tank are equally if not more important. The Examiner is however suggesting that a dual flow conduit is not necessary to achieve bottom-up freezing as alleged by counsel and the 1992 Wisniewski and Wu article proves that. The remainder of counsel's analysis blatantly ignores the combining of any teachings that one of ordinary skill would make and instead attacks the references individually as if each were applied under 35 USC 102. Ignoring the 35 USC 103 rejection as it was clearly presented to counsel is not a convincing argument.

Motivation of placing the dual flow conduit of the Kalhori and Ramadhyani in the 1992 Wisniewski and Wu device in place of the heat exchange structure shown there.

Here counsel has not traversed any of the Examiner's legitimate motivational statements. Counsel therefore concedes their validity. These statements, set forth on the last page of the office action rejection, are:

1. for the purpose of improving heat transfer (not traversed by counsel, because, it is submitted, to do so would contradict applicant's own disclosure and that of Kalhori and Ramadhyani)

2. to facilitate ease of construction (not traversed by counsel because, it is submitted, it is clearly evident that it is very easy to construct the star-shaped cooler of Kalhori and Ramadhyani (just six plates and two tubes)

3. to facilitate easy removal of the frozen mass (not traversed by counsel, it is submitted, because the Kalhori and Ramadhyani dual flow heat transfer device has no projections or holes that the ice would freeze on or freeze through that would impede its removal from the frozen mass at the end of the freezing cycle, unlike the 1992 Wisniewski and Wu device with pipes for the frozen material to envelope and get caught on.

All of these statements apply and are reinforced by the teachings of West, which counsel attacks based on the completely unsupported statement " the '642 West patent freeze products by completely different ways using completely different principles than

the present invention". In fact, West freezes the product in exactly the same way as applicant's device (by cooling with a dual-flow conduit at the center and cooling at the periphery of the container) and using the same principles, namely, cooling the product in such a manner that it uniform in consistency (i.e. applicant's desired end result avoiding cryoconcentration). Applicant has made virtually no factual showing that the products shown in the prior art freeze in anyway different from the biopharmaceuticals disclosed in the specification and vice versa. This obvious omission in applicant's case speaks volumes to the credibility of his arguments.

The previous office action is incorporated here by reference and attached to this paper as an appendix.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to John K. Ford at telephone number 703-308-2636.